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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/081,872	02/21/2002	Walter Callen	09010-108001	9897

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EXAMINER	
PROUTY, REBECCA E	

ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 05/20/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/081,872	CALLEN ET AL.	
	Examiner	Art Unit	
	Rebecca E. Prouty	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 February 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-18,47,48,74-89,92, 93,102-108,112-116 and 118-121* is/are pending in the application.

4a) Of the above claim(s) *74,108,112-116 and 118-121* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *1-18,47,48,74-89,93,102-108,112-116 and 118* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *10/03*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

The numbering of claims is not in accordance with 37 CFR 1.126 which requires the original numbering of the claims to be preserved throughout the prosecution. When claims are canceled, the remaining claims must not be renumbered. When new claims are presented, they must be numbered consecutively beginning with the number next following the highest numbered claims previously presented (whether entered or not). The current claims include two claims numbered 75. As such the second claim number 75 and claims numbered 76-120 have been renumbered as claims 76 and 77-121. All further references to claim numbers in the instant Office Action will refer to the claims **as renumbered.**

Claims 19-46, 49-73, 90, 91, 94-101, 109-111, and 117 have been canceled. Claims 1-18, 47, 48, 74-89, 92,93, 102-108, 112-116, and 118-121 are still at issue and are present for examination.

Claims 108, 112-116 and 118-121 remain withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction requirement in the response filed 6/23/03. As

amended Claim 74 corresponds to the subject matter of previously defined Group 662 and thus is withdrawn as well.

Applicants' arguments filed on 2/21/04, have been fully considered and are deemed to be persuasive to overcome some of the rejections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

Claim 4 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. The recitation of the formula in Claim 4 does not add anything to the recitation of the T_m in Claims 2 and 3 as it merely recites the known formula for calculating the T_m of a nucleic acid.

Claims 75-89, 92 and 106 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 76, 77, 87-89, and 92 are confusing in the recitation of "The probe of Claim 74" as claim 74 does not recite a probe, but instead an assay method. For purposes of

further examination, it is assumed these claims were intended to depend from Claim 75.

Claim 75 (upon which Claims 76-89 depend) is indefinite in the recitation of a nucleic acid probe … "which hybridizes to the nucleic acid target region …" as this term is unclear absent a statement of the conditions under which the hybridization occurs. Nucleic acids which will hybridize to another nucleic acid under one set of conditions may not hybridize to the same nucleic acid under other conditions. As such the scope of probes encompassed is unclear.

Claims 106 is confusing in the recitation of "host cell comprising an expression vector as claimed in claim 103" as Claim 103 does not claim an expression vector.

Claims 1-5, 7-18, 47-48, 75-89, 92, 93, and 102-107 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The rejection was explained in the previous Office Action.

Applicants submit that the claimed invention is sufficiently described in the specification so that one of

ordinary skill in the art would be able to ascertain the scope of the claims with reasonable clarity and recognize that applicants were in possession of the claimed invention. In support of applicants position applicants refer to the USPTO guidelines concerning compliance with the written description requirement of U.S.C. 112 first paragraph, specifically example 14, in which a claim reciting variants is claimed by sequence identity and function (i.e. catalyze the reaction of A to B). Based on this example, applicants suggest that these guidelines recognize that the written description requirement is met for a genus of polynucleotides described by a physico-chemical property and a defined function, and thus applicants conclude that the genus of claimed polynucleotides also meet the written description requirements of 112. Applicants argument is not found persuasive for the following reasons. First it should be pointed out that the many of the claims have no functional limitations at all. None of Claims 2-4, 17, 18, 47, 75-89, 92, and 93 require the claimed nucleic acids to encode an alpha amylase or have any other functional limitation present. As such applicants analogy to example 14 for these claims is totally inconsistent. The remaining rejected claims (i.e., 1, 5, 7-16, 48 and 102-107) do require the claimed nucleic acids to

encode an alpha amylase and thus do have a both a structural and functional limitation as found in Example 14 of the guidelines. However, these claims lack sufficient structural limitations to adequately describe the genus. As stated by applicants the requirements for written description of a genus of nucleic acids as set forth in University of California v. Eli Lilly & Co., 43 USPQ2d 1398 (Fed. Cir. 1997) may be achieved by a recitation of a representative number of DNAs defined by nucleotide sequence or a recitation of structural features common to members of the genus, which features **constitute a substantial potion of the genus**. Claims 1, 5, 7-16, 48 and 102-107 all recite nucleic acids which comprise only 35-500 residues having 85% identity to a portion of SEQ ID NO:125 (Claims 1, 5, 7-13, 16 and 102-107), or only 100 residues having 90% or 95% identity to a portion of SEQ ID NO:125 (Claims 14 and 15) as the only recited structural limitations of the claims. These recited structural features of the genus do not constitute a substantial potion of the genus as the remainder of the structure of a nucleic acid encoding a polypeptide with alpha amylase activity is completely undefined. Fragments consisting of only 35-500 residues having 85% identity to a portion of SEQ ID NO:125 or only 100 residues having 90% or 95% identity to a portion of SEQ ID NO:125 are highly unlikely

to have alpha amylase activity, constitute only a very small portion of the structure of the only disclosed species (SEQ ID NO:125) and the specification does not define the remaining structural features necessary for members of the genus to be selected. It should be noted that most of the claims which lack any functional limitation as discussed above similarly lack sufficient structural limitations as well, in particular, Claims 17, 18, 47, 75-89, 92 and 93 all lack both a functional limitation **and** sufficient structural limitations.

Claims 1-18, 47, 48, 74-89, 92, 93, 102-108, 112-116, and 118-12 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for polynucleotides encoding SEQ ID NO:126, does not reasonably provide enablement for any polynucleotide having at least 85% sequence identity to SEQ ID NO:125 and encoding a polypeptide with an alpha amylase activity or any polynucleotide comprising at least 35 bases of a sequence having 85% identity to SEQ ID NO:125, or any polynucleotide comprising a fragment of SEQ ID NO:125 or encoding fragments of SEQ ID NO:126, or all fragments and variants thereof or vectors and host cells comprising said nucleic acids. The specification does not enable any person skilled in the art to which it pertains, or with which it is

most nearly connected, to make and use the invention commensurate in scope with these claims. The rejection is explained in the previous Office Action.

Applicants argue that the specification enabled the skilled artisan at the time of the invention to identify, make and use the genus of alpha amylases claimed. Applicants refer to a declaration by inventor Jay Short, who declares that the state of the art at the time of the invention and the level of skill of the person of ordinary skill in the art was very high. Dr Short's declaration further states that one of skill in the art at the time of the invention could use the teachings of the specification and other protocols known in the art to screen for polypeptides having alpha amylase activity and that while the number of samples needed to be screened may have been high, the screening procedures were routine and successful results predictable. According to Dr. Short's declaration, knowledge of the specific structural elements which correlate with alpha amylase activity would not have been required to create variants and test them for activity. Applicants further argue that enablement is not precluded by the necessity to screen large number of compositions as long as that screening is routine. Applicants refer to *Hybritech, Inc. v. Monoclonal Antibodies,*

Inc. as support for the argument that the claimed invention is enabled even if there is a need to screen large numbers of negatives to find a sample with the desired activity.

As indicated in the previous Office Action, the specification is completely silent in regard to which are the amino acid residues which can be substituted, deleted, or inserted in the nucleic acid of SEQ ID NO:125 to obtain structural homologs of the nucleic acid of SEQ ID NO:125 as recited in the claims which encode proteins with alpha amylase activity. In addition, the specification does not provide any clue as to which 35 consecutive base fragments of the nucleic acid of SEQ ID NO:125 are required to encode proteins with alpha amylase activity nor does it provide any clue as to which fragments of a nucleic acid having at least 85% sequence identity to the SEQ ID NO:125 and encoding an alpha amylase are essential for alpha amylase activity. The prior art clearly teaches the unpredictability of assigning function based on structural homology and how small structural changes can lead to major changes in function. For specific teachings of such unpredictability, see Bork, Broun et al., Van de Loo et al., Witkowski et al. and Seffernick et al. Each of these references which are presented merely as evidence of the state of the art

as previously characterized by the examiner, shows that even small changes in the primary structure of an encoded protein can have substantial effects on function. Furthermore, it should be noted that applicants claims encompass not only nucleic acids having minor changes in structure from SEQ ID NO:125, but include nucleic acids with major changes as well. Therefore, in the absence of any information as to how structure correlates with function, one of skill in the art would have to go through the burden of undue experimentation to isolate/make the nucleic acids as encompassed by the claims, to practice the full scope of the claimed invention.

The Examiner acknowledges the ruling in *Hybritech, Inc. v. Monoclonal Antibodies, Inc* as well as the declaration by inventor Jay Short, and agrees that enablement is not precluded by the need of screening a number of compositions as long as the screening is routine. Furthermore, the Examiner agrees that creation of nucleic acids having the structural limitations recited in the claims is routine in the art. However, the Examiner disagrees with applicant's contention that testing the extremely large number of variants encompassed by the claims is not undue experimentation when there is no guidance or knowledge as to which are the structural elements in the polypeptide

encoded by SEQ ID NO:125 that correlate with alpha amylase activity. It is not routine in the art to randomly create an infinite number of variants and test them for activity. Instead, as indicated above, one of skill in the art would have some knowledge or guidance as to how structure correlates with function such that a reasonable number of variants with the potentiality of having the desired function can be created and tested. Thus, in view of the information provided, the lack of relevant examples, the lack of knowledge about the critical structural elements required for alpha amylase activity, and the unpredictability of the art in regard to accurate annotation of function based on structural homology, one of skill in the art cannot reasonably conclude that the specification is enabling for the full scope of the claimed invention.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 2, 4, 5, 7-14, 16-18, 47, 48, 75-87, 92 and 102-107 are rejected under 35 U.S.C. 102(b) as being anticipated by

Tachibana et al. (Reference AK of applicant's IDS). The rejection is explained in the previous Office Action.

Applicant's argue that the claims have been amended to overcome the instant rejection. However, it is noted that the gene disclosed by Tachibana et al. still meets all limitations of each of the instantly rejected claims. While the entire gene of Tachibana et al. does not have 85% identity to the entire sequence of SEQ ID NO:125, it clearly comprises a region of 500 nucleotides have greater than 85% identity (i.e., residues 1085-1594 of Tachibana et al. have 86.5% identity to residues 610-1140 of SEQ ID NO:125), a region of 100 nucleotides having greater than 90% identity (i.e., residues 1438-1537 of Tachibana et al. have 91% identity to residues 993-1092 of SEQ ID NO:125). Similarly while the protein encoded by the gene of Tachibana et al. does not have 90% identity to the entire sequence of SEQ ID NO:126 it clearly comprises a region of 75 amino acids having greater than 90% identity (i.e., residues 264-359 of Tachibana et al. have 99% identity to residues 266-361 of SEQ ID NO:126). As the gene of Tachibana et al. encodes an alpha amylase and comprises a region of 500 nucleotides having greater than 85% identity to SEQ ID NO:125, it anticipates all of claims 1, 5, 7-13, 16-18, 48, 75-87, 92, and 102-107. As the gene of Tachibana

et al. encodes an alpha amylase and comprises a region of 100 nucleotides having greater than 90% identity to SEQ ID NO:125, it anticipates claim 14 and as it encodes a protein which comprises a region of 75 amino acids having greater than 90% identity to SEQ ID NO:126, it anticipates claim 47.

Claims 17, 18, 47, 75-80, 87, 92, and 93 are rejected under 35 U.S.C. 102(b) as being anticipated by Lam et al. (WO 97/44361).

Lam et al. teach a polynucleotide encoding the Archaebacterium AEPIII endoglucanase which comprises an oligonucleotide of 42 consecutive nucleotides (i.e., nucleotides 256-297) with 100% identity to nucleotides 262-303 of SEQ ID NO:125.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that

was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

Claims 88 and 89 are rejected under 35 U.S.C. 103(a) as being unpatentable over Tachibana et al. (Reference AK). The rejection is explained in the previous Office Action.

Applicant has not presented any arguments specifically traversing this rejection but instead relies upon the traversal discussed above. Therefore, this rejection is maintained for the reasons presented above.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any

extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Rebecca Prouty, Ph.D. whose telephone number is (571) 272-0937. The examiner can normally be reached on Monday-Friday from 8:30 to 4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy, can be reached at (571) 272-0928. The fax phone number for this Group is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Rebecca Prouty
Primary Examiner
Art Unit 1652